Accelerated Echo Planer J-resolved spectroscopic imaging of Insular Cortex and Putamen in Obstructive sleep apnea

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Target audience: Researchers interested in obstructive sleep apnea syndrome, MRSI and accelerated imaging.

Purpose/Introduction: Obstructive sleep apnea syndrome (OSAS) is a common sleep disorder characterized by repeated apneic episodes. It is accompanied by cognitive, motor, autonomic, and affective abnormalities[1]. Although multiple brain sites are involved in the regulation of these symptoms, especially autonomic and neuropsychological behaviors, the insular cortices and putamen are key limbic structures that serve such functions. Earlier studies, mainly based on structural imaging, have demonstrated brain injury in these areas[2,3] in patients with OSAS. However, to date there are only a limited number metabolite studies using 1D magnetic resonance spectroscopy (MRS) based studies[4,5]. In this study, we examined neurochemical changes in the insular cortices and putamen of OSAS patients to provide indications of the nature of tissue changes using compressed sensing (CS) based 4D echo-planar J-resolved spectroscopic imaging (EP-JRESI)[6], which quantifies metabolites using the prior knowledge fitting (ProFit) algorithm[7]. Due to the combination of EPSI readout and increased spectral dispersion offered by 2D JPRESS, EP-JRESI enables recording better-resolved 2D spectra from multiple voxels in a single recording. Implementation of non-uniformly undersampling (NUS) and CS reconstruction further shorten the total acquisition time of EP-JRESI, making it clinically practicable. We hypothesized that metabolite integrity would be altered in a manner reflective of hypoxic injury in OSAS patients compared to healthy controls both in bilateral insular cortices and putamen.

Materials and Methods: We assessed eleven OSAS patients (54.55±10.6 years) and fourteen age matched healthy controls (HC) (50.66±8.48 years). OSAS patients were recruited following a diagnostic sleep study at the UCLA Sleep Disorders Center, based on overnight polysomonography scored according to current American academy of Sleep Medicine criteria. Evidence of clinical brain pathology was cause for exclusion. All data were collected on a 3T Trio-Tim MRI scanner (Siemens Medical Solution, Erlangen, Germany). The basic 4D EP-JRESI sequence was modified to accommodate the 25% NUS of the fully sampled data. The following parameters were used for CS EP-JRESI: TR/TE = 1.5s/30ms, 1.5x1.5x1.5 cm^3 extractable voxel resolution, $64\Delta t_1$ increments, 256 bipolar echo pair, FOV= 24x24cm^2, 2 averages, F1 and F2 bandwidths of 1000 Hz and 1190 Hz, respectively. The data first had a frequency-dependent linear phase correction applied in order to provide a maximum echo sampling scheme[7] resulting in a bandwidth of ±250Hz along F_1. The undersampled data was reconstructed using a modified Split Bregman algorithm[8] which solves the unconstrained optimization problem, $arg\ min_u \|\nabla u\|_1 + \frac{1}{2}\|F_p u - d\|_2^2$, where ∇ is the gradient operator, u is the reconstructed data, $\|x\|_n$ is the l_n norm, λ is a regularization parameter, F_p is the undersampled Fourier transform, and d is the under-sampled data.

Before applying the NUS based EP-JRESI sequence, 3D high resolution T_1-weighted images for localization were collected using a MP-RAGE pulse sequence. EP-JRESI was performed over a coronal slice covering the insular cortices and putamen. Acquired data were post-processed with a custom MATLAB-based program and metabolite ratios with respect to the 3.0 ppm creatine peak (S/S_{Cr}) were calculated using the Modified Profit algorithm. Prior knowledge generated for EP-JRESI included 20 metabolites including, creatine (Cr), N-acetylaspartate (NAA), phosphorylcholine (PCh), free choline (Cho), glycerylphosphocholine (GPC), γ-aminobutyric acid (GABA), glutamine (Gln), glutamate (Glu), glutathione (GSH), myo-inositol (mI), Nacetylaspartylglutamate (NAAG), phosphoethanolamine (PE), scyllo-Inositol (Scy), and taurine (Tau). The metabolite differences between OSAS patients and healthy controls were tested with analysis of covariance (ANCOVA) with age and gender as covariates using SPSS software. A p value < 0.05 was considered statistically significant.

Results and Discussion: Fig. 1(a) shows voxel locations on a T_1-weighted axial MRI of a 40-year-old OSAS patient brain. A representative 2D J-resolved spectrum extracted from right putamen region of the same subject and then CS reconstructed is shown in Figure 1(b). Table 1 and Fig. 1(c) show the metabolite ratios with respect to Cr in the right and left insular cortex and putamen regions of OSAS patients and healthy controls. Significantly reduced tCho/Cr was found in right insular cortex, and increased Glx/Cr, Glu/Cr in the left insular cortex and right putamen respectively. Similar trends were observed in other regions of interest. We also observed significantly increased GABA in right insular cortex. Both insular cortex and putamen showed decrease tNAA, NAA and increased mI bilaterally.

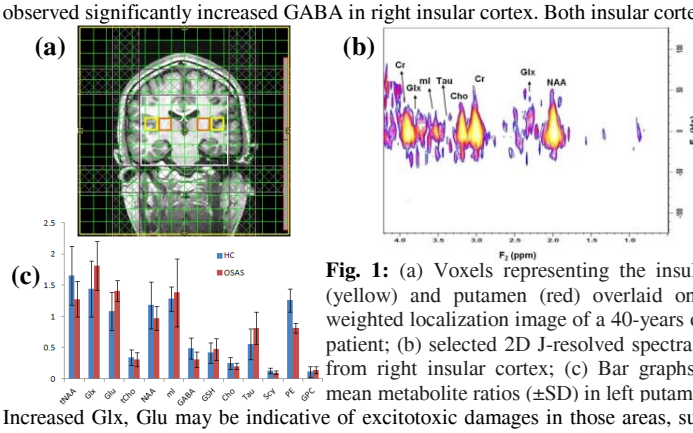

Fig. 1: (a) Voxels representing the insular cortex (yellow) and putamen (red) overlaid on the T1-weighted localization image of a 40-years old OSAS patient; (b) selected 2D J-resolved spectra extracted from right insular cortex; (c) Bar graphs showing mean metabolite ratios (±SD) in left putamen.

S/S_{Cr}	Right Insular Cortex		Left Insular Cortex		Right Putamen	
	OSAS	HC	OSAS	HC	OSAS	HC
tNAA	1.47±0.19	1.69±0.31	1.36±0.32	1.58±0.35	1.38±0.26	1.55±0.19
Glx	1.68±0.40	1.51±0.59	1.78±0.18*	1.06±0.48	1.51±0.26*	1.16±0.41
tCho	0.27±0.06*	0.34±0.06	0.29±0.07	0.30±0.09	0.29±0.09	0.33±0.07
NAA	1.24±0.17	1.42±0.42	1.11±0.40	1.19±0.29	1.25±0.29	1.22±0.23
Glu	1.23±0.37	1.01±0.33	1.55±0.24*	0.90±0.28	1.12±0.24*	0.84±0.24
mI	1.15±0.25	1.11±0.41	1.28±0.45	1.15±0.31	1.27±0.26	1.15±0.29
GABA	0.28±0.10*	0.60±0.14	0.36±0.07	0.55±0.23	0.29±0.11	0.38±0.06
GSH	0.33±0.09	0.39±0.14	0.65±0.30	0.40±0.15	0.33±0.12	0.30±0.08
Tau	0.58±0.16	0.55±0.14	0.63±0.24	0.91±0.37	0.57±0.34	0.59±0.24
GPC	0.09±0.04	0.10±0.05	0.10±0.04	0.12±0.06	0.11±0.06	0.14±0.06

Table 1: Comparison of selected ProFit-quantified metabolite ratios (Mean±SD). tNAA=NAA+NAAG, Glx=Glu+Gln; tCho=Cho+GPC+PCH.

Increased Glx, Glu may be indicative of excitotoxic damages in those areas, suggesting a potential contributor to the observed brain structural alterations in OSAS[9]. Reduced Cho/Cr and NAA/Cr ratios agree with previous 1D MRS studies obtained in the insular cortices and other regions of the brain OSAS patients[10,11]. Reduced NAA/Cr ratio is indicative of chronic neural injury in those regions, presumably consequent to known repeated episodes of hypoxia in OSAS patients[11]. Decreased tCho/Cr ratios may result from loss of myelin lipids or dysfunction of phospholipid metabolism[10]. Increased mI/Cr ratio may be a reflection of increased glial activation[4], and reactive gliosis[10] which could result in increased inflammatory action and can lead to more neuronal injury.

Conclusion: Our findings using accelerated 4D EP-JRESI are in broad agreement with the literature, and novel findings are consistent with the known phenomenon of oxidative stress in OSAS. Neuronal injury to insular cortex and putamen may contribute to abnormal autonomic and neuropsychologic functions in OSAS. The findings will help explain structural brain changes in OSAS, and suggest possible treatment options to address common central nervous system symptoms in OSAS.

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